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10/665,793

09/19/2003

Edward J. Kaplan

KAP 100 CIP

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07/28/2009

Pabst Patent Group LLP

1545 PEACHTREE STREET NE

SUITE 320

ATLANTA, GA 30309

EXAMINER

SAMALA, JAGADISHWAR RAO

ART UNIT

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1618

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|--|--|--|
| Office Action Summary | Application No. 10/665,793 | Applicant(s) KAPLAN, EDWARD J. | |
| | Examiner JAGADISHWAR R. SAMALA | Art Unit 1618 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 36-46 and 48-70 is/are pending in the application.
4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 36-46 & 48-70 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date ____. | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

The previous Office action mailed 05/26/2009 is vacated in order to consider preliminary amendment filed on 03/09/2009.

Priority

The present application, as to the claimed subject matter, one or more means structures to maintain location or orientation of the seed upon implantation selected from the group consisting of one or more biodegradable structures effective to prevent migration upon implantation of the seed in tissue, one or more biodegradable structures effective to maintain orientation in tissue and one or more compliant setal or hair structures which impart adhesive properties upon implantation into a target tissue, wherein the one or more structures effective to prevent migration or maintain orientation in tissue are selected from the group consisting of studs, knobs, ribs, fins, grapple shaped anchors, wings, stabilizers, bristles, rings, bands, hooks, knots, twists, braids, coils and combinations thereof, wherein the one or more structures prevents migration of the seed for a period of time from about 10 minutes to about three years is not described and therefore does not contain priority back to 09/861,326 or 09/861,196. The disclosure of the prior-filed application, Application Nos. 09/861,326 & 09/861,196, fail to provide adequate support for the above recited limitations, namely, the specific structures to prevent migration, in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. Thus, priority is granted to only the filing date 09//19/2002.

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The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

2. Claims 36-46, 48-50 and 52-54, 58 are rejected under 35 U.S.C. 102(e) as being anticipated by Slater et al (US 6,264,599).

Applicant claims are drawn to a seed for implantation into a subject, wherein the seed is a combination product comprising: a biocompatible carrier, one or more therapeutic components, an imaging, radiopaque, or other diagnostic marker, and one or more structures to prevent migration of the seed for a period of time from about 10 minutes to about three years.

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Slater discloses a radioactive therapeutic seeds including a substantially radiotransparent cylindrical capsule provided with a radioactive isotope, a radiopaque marker, and an engagement structure adapted to prevent axial longitudinal movement and axial rotation of a seed about its longitudinal axis when the seed is implanted (abstract). The seeds are prevented from migrating post-operatively (col.3 lines 66+). Slater discloses that it is well known in the art that the radioactive therapeutic seeds are relatively small, typically approximately 0.025 inch in diameter and approximately 0.16 inch long so that they may be implanted using minimally invasive instruments and techniques (col. 1 line 25-30). The ends of the seed capsule may be provided with connectors which can be coupled to discrete spacing links to linearly align a plurality of seeds. The spacing links may also be provided with engagement means which engages the tissue and thereby fixes each spacing link longitudinally at its location. The capsule and links can be aligned end to end to facilitate deployment and desirable relative spacing, and fixation of the capsules at the locus of treatment (col. 4 lines 6-14). In one embodiment, the engagement means is preferably a ring of hydrophobic material e.g., urethane or other expandable plastic material which causes the ring to enlarge when exposed to moisture within the human body tissue and facilitates longitudinal fixation of the seed at its implanted location. One or more laterally extending prongs, or barb-like structures may be used to provide rotational fixation as well as substantially resist axial movement of the seed within tissue and moreover, after implantation, the engagement means prevents seed migration (col. 6 lines 36-65). The exterior of the seed may be provided with indicia colored line for tracing the radioactive source (col. 6 lines 31-

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32).The seeds having engagement means such as springs may be provided with connectors at the ends thereof. The connectors such as spherical or flattened balls are adapted to couple with discrete spacing links to linearly align and hold together a plurality of seeds. The spacing links are made of bioabsorbable polymers such as d, l-poly lactide co-glycolide (col. 7 lines 10-16). Additionally, the seeds and the spacing link have moisture expandable engagement means to facilitate fixation of the seeds within the tissue and would prevent seed migration.

Since all the critical elements as required by instant claims are taught by the cited reference and claims are thus anticipated.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

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5. Claims 36-46 and 48-70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zamora et al (US 2001/0044567) in view of Slater et al (US 6,264,599), Stinson et al (US 6,251,135) and Reed et al (US 2002/0058854).

Applicant claims are drawn to a seed for implantation into a subject, wherein the seed is a combination product comprising: a biocompatible carrier, one or more therapeutic components, an imaging, radiopaque, or other diagnostic marker, and one or more structures to prevent migration of the seed for a period of time from about 10 minutes to about three years.

Zamora discloses a brachytherapy device comprising a biocompatible biodegradable component (i.e. polymeric material), a non-radioactively therapeutic component and a biodegradable radiopaque marker (see abstract). The biodegradable component includes polymers (e.g. Poly (D, L-lactide) poly (L-lactide), (polyglycolide, poly (L-lactide-co-glycolide) that are same as those claimed (0025 and 0055). The biocompatible polymer such as poly (hydroxybutyrate) is included that can read as biocompatible elastic carrier to form an elastic brachytherapy device (0049) since they are essentially same compounds. The size and shape of the devices are within the scope of those claimed (0057). Fabrication methods and techniques permit the construction of brachytherapy devices having a variety of forms, including devices sized the same as art conventional devices commonly used in brachytherapy (0029). The non-radioactive therapeutic component includes chemotherapeutic agent such as cisplatin bleomycin, a radiosensitizer drug such as 5-halo uracil compounds (0080). Zamor also teaches the radiopaque marker which includes various markers that are

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biodegradable such as platinum, tantalum and bismuth (0051), where these markers are same as one required by claims, thus non-radionuclide imaging marker requirement is inherently met. The seeds of the device may be implanted singly, or may utilize suture strands, webs, meshes or other means to group the devices in a desired manner (0085). Additional disclosure includes, that the improved delivery devices deliver local radiation, and optionally local chemotherapeutic or bioactive drugs, and are degradable after implantation so that the devices largely or completely disappear from the treatment region over time.

Zamora fails to disclose one or more biodegradable structures to prevent migration of the seed, and a seed is in a magazine or cartridge

Slater discloses a radioactive therapeutic seeds including a substantially radiotransparent cylindrical capsule provided with a radioactive isotope, a radiopaque marker, and an engagement structure adapted to prevent axial longitudinal movement and axial rotation of a seed about its longitudinal axis when the seed is implanted (abstract). The seeds are prevented from migrating post-operatively (col.3 lines 66+). The ends of the seed capsule may be provided with connectors which can be coupled to discrete spacing links to linearly align a plurality of seeds. The spacing links may also be provided with engagement means which engages the tissue and thereby fixes each spacing link longitudinally at its location. The capsule and links can be aligned end to end to facilitate deployment and desirable relative spacing, and fixation of the capsules at the locus of treatment (col. 4 lines 6-14). One or more laterally extending prongs, or barb-like structures may be used to provide rotational fixation as well as substantially

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resist axial movement of the seed within tissue and moreover, after implantation, the engagement means prevents seed migration (col. 6 lines 36-65).

Stinson discloses an implantable endoprosthesis and radiopaque marker system. The marker system includes an implantable endoprosthesis having a tubular and radially expandable structure adapted to be disposed in a body lumen and at least one elongated marker. The marker includes a radiopaque material having a proximal end, a distal end, a thickness (col. 5 lines 54-60). The markers may be deformed by plastic deformation, elastic deformation, or combinations thereof and may include a twist, coil, knot, crimp, weld, and combinations thereof (col. 6 lines 10-25). The ends of the markers may be tied, twisted, knotted, welded or adhesively connected together and thereafter clipped and positioned to lie in an unobtrusive low-profile position.

Reed discloses a device for dispensing implantation seeds from a seed magazine, comprising a body, seed magazine receiving and locating means, seed dispensing means for ejecting seeds from a seed magazine, and the loader body further defines a seed cartridge port for receiving a seed cartridge having a seed dispense port (abstract and 0007).

It would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate brachytherapy seeds having one or more biodegradable structures to prevent migration of seeds upon implantation into a target tissue disclosed by Zamora. The person of ordinary skill in the art would have been motivated to make these modification because Slater teaches that radioactive seeds having one or more engagement structures of various forms would prevent migration of seeds upon

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implantation i.e., as the seeds are released from the needle, the engagement means (structures) expand and positively engage the tissue at their respective release sites. As a result, even if there is some proximal movement of the obturator relative to the implant site, any negative pressure created between the obturator and the seeds will not overcome the engagement of the seeds in the tissue and the seeds remain at their intended location and moreover, after implantation, the engagement means prevents seed migration and reasonably would have expected success because it is well known in the art that the biodegradable structures of various forms for fixation of the device in the host tissue so that it remains in place after implantation for the duration of the radiation treatment, and possibly indefinitely.

Response to Arguments

Applicant's arguments filed on 03/09/2009 have been fully considered but they are not persuasive.

Applicant asserts that Zamora does not disclose or suggest structures attached to the seed to maintain its position and/or orientation as required by the claims.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combination of references. See *in re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *in re Merck & Co.*, 800 F.2d 1091, 231 USPA 375 (Fed.Cir.1986).

In this case, the Zamora patent is relied upon to show that it is known in the art to manufacture radioactive seeds for interstitial radiotherapy of malignant neoplasms or

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other diseases treatable with radiation. Zamora discloses method and improved delivery devices to deliver local radiation, and chemotherapeutic or bioactive drugs, and after implantation so that the radioactive source material localized at the site of implantation at all times while emitted radiation remains significant (0029). The outer surface of devices, however, have sufficient permanence or persistence so that the radioactive source material remains localized at the site of implantation at all times while the emitted radiation remains significant. The brachytherapy devices disclosed by Zamora are made such that the density of the device approximates that of normal and cancerous tissues or frequently have a greater density than that of the tissue within which they are placed. By approximating the density of the tissue in which the devices are placed, movement of the devices within the body is minimized (0083). And thus, the device disclosed by Zamora would obviously retain integrity throughout the period of active emission of radiation.

Applicant also asserts that Zamora does not disclose a degradable radiopaque marker.

This argument is not persuasive since, Zamora does disclose radiopaque material capable of being detected by X-rays and conventional radiographic methods. Preferred iodine-containing radiopaque agents include iodixanol, iohexol, iodophthalein sodium, and metal containing contrast agents such as barium sulfate and bismuth trioxide, which can be mixed with polymers such as polyurethane to increase radiopacity and the like (0051).

Applicant also asserts about "Long Standing Need and Commercial Success" of the seeds.

The relevance of long-felt need and the failure of others to the issue of obviousness depend on several factors. First, the need must have been a persistent one that was recognized by those of ordinary skill in the art. In re Gershon, 372 F.2d 535, 152 USPQ 602,605 (CCPA 1967). The alleged problem in this case is migration of seeds from the implantation site, and the prior art also discloses the brachytherapy devices capable of retaining integrity throughout the period of active emission of radiation (i.e., minimizes the chance of migration of implanted seeds within a patient's body). And further, the invention must in fact satisfy the long-standing need. In re Cavanagh, 436 F.2d 491,168 USPQ (CCPA 1971).

Objective evidence of nonobviousness including commercial success must be commensurate in scope with the claims. In re Tiiffin, 448 F.2d 791,171 USPQ 294 (CCPA 1971). In order to be commensurate in scope with the claims, the commercial success must be claimed features, and not due to unclaimed features. Joy Technologies Inc. v. Manbeck, 751 F. Supp.225, 229, 17 USPQ2d 1257, 1260 (D.D.C. 1990), aff'd, 959 F.2d 226,228, 22 USPQ2d 1153, 1156 (Fed. Cir. 1992)

The instant claim 36, a seed for implantation into a subject, wherein the seed is a combination product comprising a biocompatible carrier, one or more therapeutic components, an imaging, radiopaque, or diagnostic marker, and one or more structures to maintain location or orientation of the seed upon implantation. The claim does not say anything about anchor seed and the feature recited in the commercial success product

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is for anchorseed designed to help reduce seed misalignment and seed migration. The examiner does not know the composition of the anchorseed and also to compare it with the instant claims.

An affidavit or declaration attributing commercial success to a product or process "constructed according to the disclosure and claims of [the] patent application" or other equivalent language does not establish a nexus between the claimed invention and the commercial success because there is no evidence that the product or process which has been sold corresponds to the claimed invention, or that whatever commercial success may have occurred is attributable to the product or process defined by the claims. *Ex parte Standish*, 10 USPQ2d 1454, 1458 (Bd. Pat. App. & inter. 1988). Furthermore, the success of an embodiment within the claims may not be attributable to improvements or modifications made by others. *In re Vamco Machine & Tools, Inc.*, 752 F.2d 1564, 224 USPQ 617 (Fed. Cir. 1985).

Other arguments presented by applicant are moot in view of the new grounds or rejection set forth above.

Double Patenting

Claims 36-40, 45, 47-55 are rejected on the ground of nonstatutory obviousness type double patenting as being unpatentable over claims 1-3, 5, 10, 12, 13, 30, 32, 35, 38 and 41 of US 6,746,661 B2 **are maintained** for reasons of record in the previous office action filed on 09/30/3008.

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Applicant asserts that brachytherapy seeds formed of biodegradable polymer have elastic properties and other distinct structures for maintaining the location of the seed.

This argument is not found persuasive since the polymers used in the instant claims and polymers disclosed in US 6,746,661 are biodegradable polymers and would have the elastic properties. And further, the US 6,746,661 is silent about the migration of seeds from the implantation site (for maintaining the location of the seed). Thus, the instant claim is within the scope of the claim of the US Pat. 6,746,661. Thus scope is overlapping each other and properly included in the rejection because they are patentably distinct from each other. Thus, the claim is readily envisaged by the teaching of the prior art and the claim is properly included in the rejection. Accordingly, ODP is maintained.

Conclusion

1. No claims are allowed at this time.
2. Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAGADISHWAR R. SAMALA whose telephone number is (571)272-9927. The examiner can normally be reached on 8.30 A.M to 5.00 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571)272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

Jagadishwar R Samala
Examiner
Art Unit 1618

sjr